



Case report

Sudden death of a young woman attributed to diabetic ketoacidosis



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ABSTRACT

A young woman's death at home was attributed to new onset diabetic ketoacidosis with subsequent litigation supported by several expert consultants, despite a history and postmortem findings inconsistent with this diagnosis. More thorough tissue study of the heart and analysis of the circumstances led to a credible explanation of the entire scenario.

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1. Introduction

An 18½ year-old woman was found at 7 AM by her mother, lying on the floor on her side, wedged between the floor and the bed. She was completely unresponsive, with blue lips, but still warm. The EMS team arrived within minutes but failed to resuscitate her. They found her blood sugar level to be very high (absolute value not reported).

Her medical history in the 4 years before her death included treatment for nodulocystic acne with isotretinoin for approximately 6 months, oral contraceptive therapy from age 16, and 3 monthly Depo-Provera at the time of death. She used an albuterol inhaler as needed for asthma. Three weeks before her demise, she had incision and drainage for an abscess in the right buttock, which grew candida and was treated with diflucan. Healing was uneventful.

Her weight was 162 pounds when she had a sports physical at age 15, 189 pounds when she was seen for her acne a year later, and at a physical examination for work at age 17, she weighed 199 pounds. She began a healthier diet and exercise program and 8

months later, 9 months before her death, she weighed 135 pounds. She weighed 130 pounds at her last medical encounter 3 weeks before her death, which was between the 50th and 75th percentile for her height.

Her MySpace entry a week before death described her excitement about impending graduation from high school. An earlier entry described how healthy she felt after recovering from her abscess. An entry 3 days before her demise was equally exuberant and devoid of any complaint.

The day before her death, she awoke with diarrhea, vomiting, and fatigue, and went back to bed. In the evening she was feeling very tired. She was given NyQuil so she could sleep because she was restless, and she was also given an unknown amount of acetaminophen (Tylenol). Her breathing was a bit labored but alleviated by her inhaler, which the parents observed her using once that evening. She was also noted to use the bathroom only once that evening.

At autopsy, done the day after death, she weighed 123 pounds. Vitreous glucose concentration was 485 mg/dL, ketones 25 mg/dL, blood acetone 16 mg/dL, and the urine was positive for numerous drugs which were never specifically identified. Vitreous concentrations of glucose greater than 200 mg/dL and ketones above 10 mg/dL have been considered indicative of DKA.¹ Blood ethanol level was 0.03%. There were numerous contusions to the extremities and head but no internal trauma seen. There was glycogenization of hepatic

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nuclei, and vacuolization of renal tubular epithelial cells. The cause of death was determined to be “diabetes mellitus with diabetic ketoacidosis”.

2. Litigation

Because she was seen 3 weeks before death and no tests done to determine if she had diabetes, a malpractice suit was filed. A number of expert opinions supported this action:

- A pediatric endocrinologist said that he was adamant that the standard of medical care would have been for the primary care physician to obtain a fasting blood sugar in view of the rectal abscess and 70 pound weight loss. “I have no doubt that had she been diagnosed and treated with insulin, even as late as on the day before her death, she would have survived”.
- An adult endocrinologist from a premier diabetes clinic also invoked weight loss and the candida abscess of the buttock, and stated, “I believe she developed her diabetes [a year earlier]. Had her diabetes been diagnosed and treated on or before [the date of her abscess treatment] she would be alive today”.
- A practicing pediatrician concurred that her dramatic weight loss and candida abscess were clear indications that she had undiagnosed diabetes.
- A professor and chairman of pathology reviewed the records, the death certificate, the autopsy report, and the autopsy slides at the invitation of the plaintiff’s attorney. He noted that the 80 pound weight loss over a period of 2 years was consistent with diabetes. He was unable to identify any inflammation in the pancreatic islets. He considered that her cardiac arrest was “consistent with a sudden arrhythmia which was most likely the result of hyperkalemia and other metabolic perturbations associated with diabetic ketoacidosis”, despite noting that that there was no way to assess potassium levels postmortem. He noted that, “There were no other findings, either in the tissue pathology, or the toxicology, that could provide an alternative cause of her sudden death”.

3. Case closed?

There were obvious problems with the diagnosis of diabetic ketoacidosis (DKA) causing the death of this young woman and the explanations provided by experts:

- Deposition testimony of her parents and several of her friends, and her online diary, testified to good health and spirits without any symptoms to suggest diabetes until the day before her death.
- Her impressive weight loss occurred long before her demise and was the result of a concerted effort to attain normal weight. In fact, from 9 months before her death until 3 weeks before, she lost only 5 pounds, within the range of measurement reliability. From 3 weeks before her death to autopsy, the weight difference was 7 pounds (5%), some of which would be attributable to the difference between being weighed with clothes on in the clinic in March in a northern clime and unclothed at autopsy. Some dehydration would also be expected with her acute illness. At worst, this would not be sufficient acute weight loss to invoke fatal ketoacidosis. Her extreme weight loss 9 months earlier in the absence of any typical symptoms of diabetes (polyuria, polydipsia, polyphagia, fatigue) at the time or later, before her demise, along with the absence of recent significant weight loss, fail to support the supposition of a fatal episode of DKA.

- The unremarkable healing of her buttocks abscess, which may have been due to Depo-Provera injection, would be inconsistent with untreated diabetes.
- Her terminal illness was characterized by diarrhea and vomiting, indicative of gastroenteritis; the vomiting of diabetic ketoacidosis is not accompanied by diarrhea. Nor was she as severely dehydrated as would be expected with fatal DKA, as indicated by her weight and vitreous urea nitrogen (22 mg/dL) and creatinine (1.4 mg/dL).
- Neither plaintiff nor defense pathology consultants found inflammatory change in the pancreatic islets, which would be inconsistent with recent onset diabetes.²
- The extensive bruising described at autopsy was not explicable by the hypothesis of terminal DKA. The parents testified that she had no bruising the evening before.
- The glycogenization of hepatic nuclei and vacuolization of renal tubular epithelial cells were not explained by DKA.
- The blood-alcohol level of 0.03% also could not be explained by DKA.

4. Further tissue study

The second outside pathologist found that a section of the heart from the right ventricle was remarkably thin with areas in which adipose tissue was infiltrating and replacing myocardial fibers. Slides were sent to a professor of medicine and physiology occupying a chair in cardiovascular research, with a particular interest and extensive bibliography in cardiac arrhythmias and sudden cardiac death. He confirmed marked fatty infiltration in the right ventricle extending through the wall of the ventricle almost to the endocardium in some places with a small amount of fibrosis in the right ventricle, diagnostic of arrhythmogenic right ventricular dysplasia (ARVD). This disorder affects individuals of this age, accounting for 20% of sudden fatal cardiac events in young people and athletes.³ Although approximately 50% of cases of ARVD are familial, no family history of sudden death or cardiac arrhythmias was noted in the medical records and family studies for undiagnosed ARVD were not pursued.

5. Role of NyQuil

The only explanation for the alcohol concentration in the blood would have been ingestion of NyQuil, which is a 10% alcohol suspension. Ingesting the entire 10 ounce bottle, she would have received a quantity of alcohol equivalent to twice that found in an equivalent quantity of high alcohol beer, which could result in the blood-alcohol level recorded or greater for at least 4 h.⁴

Also contained in this quantity of NyQuil would be 10 g of acetaminophen, enough to damage the liver⁵ and the renal tubules,⁶ particularly considering that she also received an unknown quantity of acetaminophen as Tylenol. Acetaminophen poisoning has also been associated with hyperglycemia and acidosis.^{7,8} She would have also consumed 300 mg of dextromethorphan which can substantially depress the central nervous system and produce clumsiness, dizziness, ataxia, and hallucinations.⁹ A third component, doxylamine succinate, is an anti-histamine with atropine like affects which would have been consumed in a quantity (125 mg) sufficient to cause disorientation, agitation, and conduction delays in the heart.¹⁰ Finally, pseudoephedrine can also produce agitation to the point of acute psychosis, seizures, and cardiac arrhythmias, including heart block.¹¹ With presumed ingestion of the entire bottle of the pre-2006 formulation of NyQuil, as evidenced by the alcohol concentration, she would have received 600 mg of pseudoephedrine, 10 times the adult dosage. This large dose of a

catecholamine-like drug would also likely result in insulin resistance with hyperglycemia, as has been documented in mice.¹² Catecholamines are considered to be important counter regulatory hormones (i.e. counter regulatory to insulin) in the pathogenesis of diabetic ketoacidosis, their excess causing increased glucose production and lipolysis leading to ketogenesis and acidosis.¹³

6. Putting it all together

The blood-alcohol level and hepatic and renal damage were indicative of ingestion of the entire bottle of NyQuil and an unknown additional quantity of acetaminophen. Confusion, agitation, and loss of coordination as a result of the alcohol and drugs in NyQuil would have resulted in staggering and stumbling that would explain the bruising. Hyperglycemia and ketoacidosis could have been the result of a combination of starvation ketosis and acetaminophen poisoning, reinforced by pseudoephedrine. The most important toxic effects of the drugs in NyQuil were likely those affecting the abnormal heart, resulting in cardiac arrhythmia and irreversible cardiac arrest, the terminal outcome consistent with the finding of advanced ARVD.

Ethical approval

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Conflict of interest

No potential conflict of interest.

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